Wright nebulizer and the aerosol is administered continuously for two minutes. After each serial concentration, FEV_1 values are determined, and the procedure ends when there is a 20% or greater fall in the FEV_1 value compared with baseline. Results are expressed as either the provocative dose of methacholine producing a 20% decrease in FEV_1 (PD_{20}), the cumulative dose in breath units (1 breath unit = 1 inhalation of 1 mg per ml of methacholine) producing a 20% decrease in FEV_1, or the area under a dose-response curve. More than 90% of those with asthma respond to methacholine by 200 breath units. Bronchoconstriction following the inhalation of methacholine may also develop in persons with allergic rhinitis, chronic bronchitis, bronchiectasis, and cystic fibrosis, indicating airways hyperreactivity; the provocative or cumulative dose is often larger, however.

Methacholine challenge can be associated with severe bronchoconstriction and should be administered only if oxygen, resuscitation equipment, and inhaled and parenteral bronchodilators are available. It is not a test for routine office use but a useful tool for the evaluation of a person with unexplained respiratory tract symptoms.

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Management of Chronic Idiopathic Urticaria

URTICARIA (HIVES) IS A PRURITIC MIGRATORY ERUPTION characterized by edematous, erythematous wheals of various sizes in the superficial dermis. The term "chronic" refers to symptoms of six weeks' duration or more. Angioedema is a similar reaction confined to the deeper dermis and subcutaneous tissue. The causes of urticaria and angioedema include food, drugs, infection, inhalants, bites and stings, contactants, physical agents, neoplasms, connective tissue disease, and psychic factors. Fatalities from laryngeal edema have been limited almost exclusively to patients with hereditary angioedema and edema due to Hymenoptera stings. Allergy immunotherapy can also result in death. The cause of chronic urticaria usually is not known, hence the term chronic idiopathic urticaria.

For this discussion it is assumed that possible causes have been considered and avoidance has been attempted. Such avoidance may include a diet free of salicylates, benzoic acid derivatives, and tartrazine yellow No. 5, although their potential role in the etiology is controversial. Additionally, potentiating factors such as alcoholic drinks, aspirin, exertion, and heat generally should be avoided. Most patients respond to symptomatic therapy, of which antihistamines of the H_1 inhibitor type are the therapeutic mainstays. Hydroxyzine hydrochloride (Atarax, Vistaril), diphenhydramine hydrochloride (Benadryl), and cyproheptadine hydrochloride (Periactin) are the most effective. Of the three, hydroxyzine is the most potent, with recommended doses starting at 10 to 25 mg four times a day with upward titration. With excessive daytime sedation, 25 to 100 mg can be given at bedtime. Terfenadine (Seldane) with doses as high as 60 mg taken four times during the day can be used in combination with the more sedating H_1 antihistamines. Astemizole (Hismanal) just became available in the United States. It has an exceptionally long duration of action. This and another agent under investigation, ketotifen fumarate, might prove to be useful in refractory patients. Combination therapy should be attempted when single agents are insufficient. Cimetidine, an H_2 blocker, in combination with the H_1 antihistamines, can prove more effective than an H_1 antagonist alone in certain patients. Doxepin, an antidepressant with both H_1- and H_2-blocking properties, is potent in vitro and in vivo and can be given at doses of 25 to 75 mg at bedtime.

Sympathomimetic agents such as terbutaline sulfate, 2.5 to 5 mg three times a day, can supplement the antihistamines. In this respect it should be recalled that patients with acute, severe urticaria or angioedema often respond to subcutaneously administered epinephrine, 0.3 ml of 1:1,000 solution for adults. If the disease is severe and not responding to other forms of treatment, corticosteroids may prove useful. After an initial oral boost such as 45 to 60 mg daily for three to six days, tapering and alternate-day doses, such as 15 to 20 mg every other day, sustain the beneficial effect. Continuous steroid therapy is rarely necessary.

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Asthmogenic Drugs

ASTHMA IS A MULTIFACTORIAL DISEASE characterized by abnormal bronchial reactivity and may be perceived as wheezing, cough, chest tightness, or shortness of breath. Drugs may affect this hyperreactivity by any of several mechanisms. For example, drugs may alter bronchial reactivity through an immunoglobulin (Ig) E-mediated allergic mechanism or by the direct pharmacologic effect of a drug. We will focus on the second group of adverse reactions because they are repeatedly implicated in provoking occult or quiescent asthma and in increasing the severity of established asthma.

Foremost in this drug class are the β-adrenergic receptor blockers, which produce bronchoconstriction by directly blocking the β-receptor on the bronchial smooth muscle. This group currently has three main subclasses in clinical use: nonselective β-blockers such as propranolol or nadolol; β_1-selective (cardioselective) β-blockers—metoprolol, atenolol, for example; and β-blockers with intrinsic sympathomimetic activity, that is, partial agonists such as pindolol. All three classes have been shown to produce deleterious effects. Clearly, the first class produces bronchospasm at the lowest levels and should be avoided in patients with asthma wherever possible. The second was introduced partly because of this limit within the first class. The degree of effect on the β_1- versus β_2-receptors is relative, however, and a large enough dose of a selective drug will still produce significant β_2-blockade. The properties of the third group are less clear;